Atopic dermatitis: Update on Management

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Organizational:
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NIH Food Allergy Guidelines Expert Panel

Disclosures: Jennifer S. Kim, MD

None

Learning Objectives

Upon completion of this workshop participants should be able to:

1. Describe treatments for atopic dermatitis including skin care, application of dressings, and bleach baths.
2. Review patient education tips for caring for atopic dermatitis.

Overview

- Definition
- Treatment
  - Skin care – Soak and seal
  - Anti-inflammatory agents
  - Antibiotics
  - Antipruritics
  - Education
- Triggers

Epidemiology

- Eczema is on the rise: since WWII keeps increasing in developed countries
- Up to 20% of all children get some eczema
- Usually starts early
  - By 1 year of age in 60%
  - By 5 years of age in 85-90%
- Frequently outgrown

What causes it?

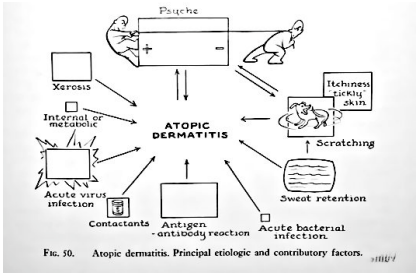


Fig. 50. Atopic dermatitis. Principal etiologic and contributory factors.

Pillsbury DM, Kligman AM, Shelley WB. *A manual of cutaneous medicine, by Donald M. Pillsbury, Walter B. Shelley [and] Albert M. Kligman. Philidelphia. Saunders, 1961.*

Etiology

- "Eczema" is Greek for "result of boiling over"
- "Atopic" ~ Allergic
  - >50% develop asthma
  - ~75% develop allergic rhinitis

KEY FEATURES:

Red, **itchy**, scaly/flaky, sometimes oozing rash
Chronic and relapsing condition

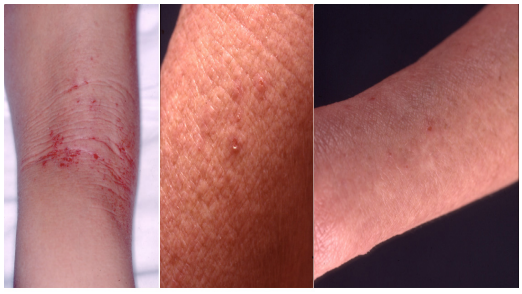
***ITCH is critical for diagnosis.**

Clinical features of AD

Major features

- Pruritus
- Facial and extensor involvement in infants and children
- Flexural lichenification in adults
- Chronic or relapsing dermatitis
- Personal or family history of atopic disease

Lichenification



Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 6e

Clinical features of AD

Major features

- Pruritus
- Facial and extensor involvement in infants and children
- Flexural lichenification in adults
- Chronic or relapsing dermatitis
- Personal or family history of atopic disease

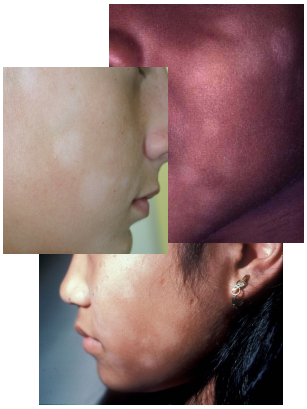
Minor features

- Xerosis
- Cutaneous infections
- Ichythosis, palmar hyperlinearity, keratosis pilaris
- Pityriasis alba
- White dermatographism and delayed blanch response

Pityriasis Alba

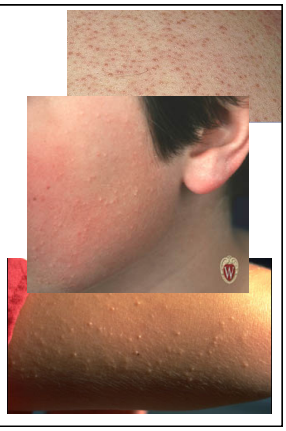
- Asymptomatic hypopigmented patches on face, upper extremities, neck upper trunk
- More prominent in summer (won't tan well)
- Dry skin care, sunscreen, reassurance (can take months to resolve)

Tx: Low potency steroids or calcineurin inhibitors BID for 1-2 weeks

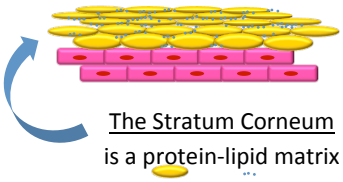


Keratosis Pilaris

- Variant of normal skin
- May improve with age
- Cosmetic issue
- Distribution: extensor surfaces of upper arms, anterior thighs, lateral cheeks, buttocks
- No referral needed… treatments ineffective in the long term



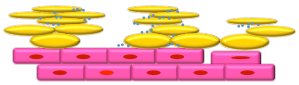
What goes wrong in AD?
Normal Epidermis Serves as a Barrier



Protects against water loss & allergen/ microbe entry

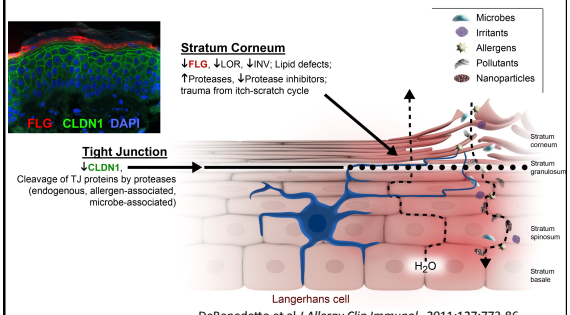
The Stratum Corneum
is a protein-lipid matrix
with filaggrin, ceramide, and sphingosine

Defect in Epidermal Barrier Function is Hallmark of AD



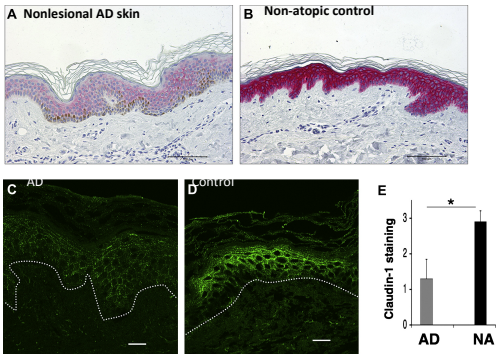
- **Filaggrin** loss-of-function mutations (R510X and 2282del4): associated with ↑risk of AD, asthma associated with AD, peanut allergy, and allergic rhinitis
  (Palmer CN et al. *Nature Genetics*, 2006; Weidinger S et al. *JACI*, 2008)
- Altered sphingolipid metabolism → decreased **ceramide** and sphingosine correlates with increased *S. aureus* colonization
  (Arikawa, J et al. *J Invest Derm, 2002)*
- ↑ trans-epidermal water loss

Stratum Corneum + Tight Junctions
2 barrier structures

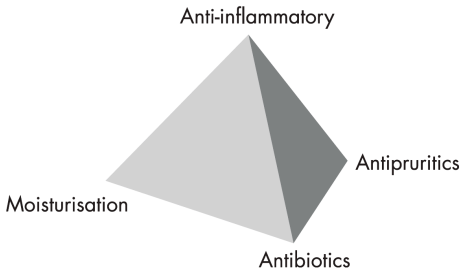


DeBenedetto et al *J Allergy Clin Immunol* 2011;127:773-86

Claudin-1 expression is reduced in AD



How to treat atopic dermatitis



Excellent skin care is the cornerstone of successful AD management

Combat Dryness

- Barrier function impaired
- Skin's ability to lose water increased
- Skin's ability to bind water decreased

Bathing: wet or dry?

Benefits

- Greater penetration of topical therapies
- Debride infected eczema

Drawbacks

- May further dry skin
- Water evaporation causes disruption of skin barrier

"SOAK and SEAL" method

- Bathe 1-2 times DAILY
- Soak 10-15 minutes in lukewarm water
- Use moisturizing cleanser where needed
  Olay Moisturinse, Aveeno Advanced Care Wash

Bathing <u>without</u> moisturizers compromises skin hydration

Immediately After Bath

- GENTLY pat skin dry
  No rubbing!
- Apply topical steroid first
- Apply moisturizers liberally
- Apply wraps if needed

Emollients

- Ointment = pure grease
- Cream = grease with some water
- Lotion = water with some grease

***The best moisturizer is one they will use!**

Moisturizers: a **key** part of the bathing routine

- Reapply frequently
  – at least TWICE daily
- Establish routine
  – Apply at every diaper change
  – Apply every time after washing hands
- May use different moisturizers in AM vs for and adults

Barrier Creams

Pros

- Non-steroidal
- Moisturizing and barrier repair effects
- Anti-pruritic actions

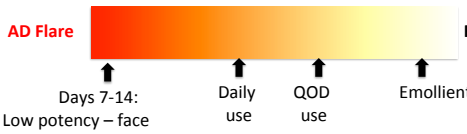
Cons

- Requires prescription
- **Relatively expensive**
- Not always covered by insurance

Approved by FDA as medical devices

Anti-inflammatory Treatment

Topical Steroid Application



Aim for RARE FLARES

Leung DY, Nicklas RA, Li JT, et al. Disease Management of Atopic Dermatitis: an updated practice parameter. Ann Allergy Asthma Immunol 2004;93:S1-S27
Krakowski AC, Eichenfield LF, Dohil MA. *Pediatrics* 2008 Oct 122(4):812-24

Treatment of Inflammation

- Primary goal of therapy
- If this step is skipped, failure will occur
- Topical steroids still the mainstay of therapy
- Extremely safe when used correctly

Use topical steroids to
"put out the fire"

Topical Corticosteroids

- **First-line** treatment for flares
- Potency classification
  - Class I – most potent
  - Class VII – least potent (i.e., hydrocortisone)
- Potencies differ and can be confusing
- Vehicles differ and may affect acceptance, potency (oils, cream, ointments), and absorption as well as side effects
- Ointments are best for chronic dry skin

Which one? Where?

Face (Class VI or VII)

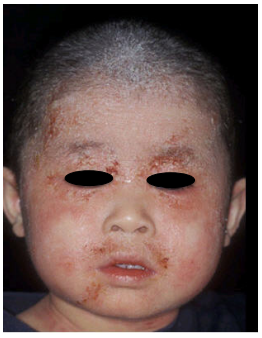
- VII: hydrocortisone 1% or 2.5% ointment
- VI: aclometasone diproprionate 0.05% ointment
- VI: desonide 0.05% gel, ointment

Body (class II or lower)

- IV: hydrocortisone valerate 0.2% ointment
- IV: mometasone furoate 0.1% cream
- III: triamcinolone acetonide 0.1% ointment
- II: mometasone furoate 0.1% ointment

Don't Forget the Scalp!

- Often involved in AD
- Oil, lotion, foam, gel easy to apply to scalp
- Mid-low potency steroid nightly when flaring



Steroid Side Effects Are Rare!

- Reversible
  - Telangiectasia/prominent blood vessels
  - Atrophy/thin skin
  - Acne/rosacea
  - Increased hair growth
- Non-reversible
  - Stretch marks

Myths About Steroids

"Steroids will stunt my child's growth"

- Low to mid potency steroid will not cause clinically significant adrenal suppression

"Topical steroids can only be used for 5-7 days then discontinued."

- Avoid side effects by the *"The Touch Rule"*
  - ✓Use steroids on rough skin until smooth.
  - ✓Then stop and only use emollients.

Topical Steroids – Pearl

For patients saying

"As soon as I stop, it comes RIGHT BACK"

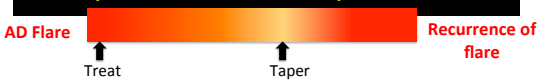
or

"I have to use it EVERY DAY"

then steroid potency is probably too low*

*provided all other areas of the tetrad are being maximized

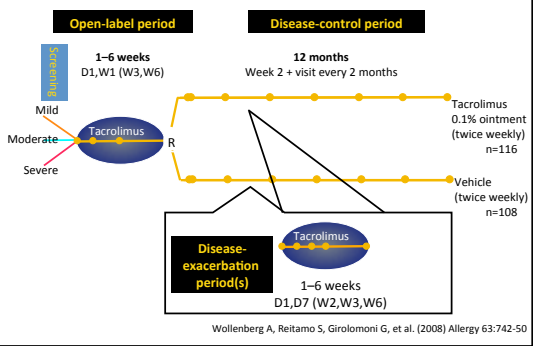
For patients with frequent flares



- Fluticasone propionate cream 2 or 3 times weekly to areas usually affected (OFF LABEL)
- Topical calcineurin inhibitors
  - Intermittent short courses
  - Facial and periocular AD
  - Proactive (OFF LABEL) usage: 2-3x/week to areas typically affected by AD

Wollenberg A et al Allergy 2008;63:742-750; Paller AS et al Pediatrics 2008;122: e1210-e1218
Breneman D et al J Am Acad Dermatol 2008;58:990-9; Thaci D et al Br J Dermatol 2008 De:

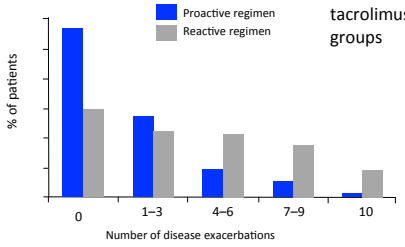
Proactive therapy - Study design



Wollenberg A, Reitamo S, Girolomoni G, et al. (2008) Allergy 63:742-50

Proactive therapy

Proactive therapy yielded significantly less disease exacerbations ($p < 0.001$)



- Similar results were seen in all severity strata
- Similar amounts of tacrolimus used in both groups

Topical Calcineurin Inhibitors

- 1/19/06: Black box warning for theoretical risk
- No evidence of increased incidence of skin cancer, lymphoma in humans
- Systemic absorption low
- Long term data needed

Fonacier L et al. *J Allergy Clin Immunol* 2005 115(6):1249-53
Berger TG et al. *J Am Acad Dermatol* 2006 54(5):818-23.
Arellano FM et al. *J Invest Dermatol* 2007 127(4):808-16
Undre NA et al. *British Journal Dermatol* 2009 160:655-9.

Topical Calcineurin Inhibitors

- Non-steroid topical immunomodulators
  - Tacrolimus (Protopic) ointment (mod-severe AD)
    - 0.1% (>15 yr), 0.03% (>2 yr)
  - Pimecrolimus (Elidel) cream (mild-mod AD)
    - 1% (>2 yr)

Topical Calcineurin Inhibitors

Advantages

- Steroid-free for thin skin areas: face, eyelids, perioral region, genital area, axillary region, or inguinal folds
- No worry of steroid side effects

Disadvantages

- Transient burning or stinging with initial application (lasts 1 week)
- Less effective for flare of eczema, severe disease

How much to Dispense?

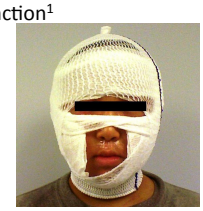
Area Treated*	Once	BID x 1 wk
Hands, face	2 gm	28 gm
Leg	4 gm	56 gm
Entire body	30 gm	420 gm

*70 kg adult

Lynfield YL, Schechter S. *J Am Acad Dermatol*. 1984 10(1):56-59

Wraps for flares of AD

- Recovery of epidermal barrier function[1]
- Bathe & apply topical steroids[2,3]
  - Bottom wet layer & dry upper
  - Apply overnight
- Zinc oxide wrap



Ref. 1. Lee JH et al. JEADV 2007 21:1360-1368
2. Nicol NH, Boguniewicz M. *Dermatology Nursing* Oct 2008
3. Krakowski AC, Eichenfield LF, Dohil MA. *Pediatrics* 2008 **122**(4):812-24

Wet Wraps

- Face: 2 to 3 layers of wet gauze held in place with tubifast or other dressing
- Arms/Legs: Tube socks or gloves; cover with dry clothing
- Total body: one layer of wet clothing - pajamas, long underwear, turtleneck tops covered by dry pajamas or sweat suit

Wet Wrap Advantages

- Skin re-hydration
- More restful sleep
- Reduced redness and skin inflammation
- Diminished itching
- Avoidance of hospitalization

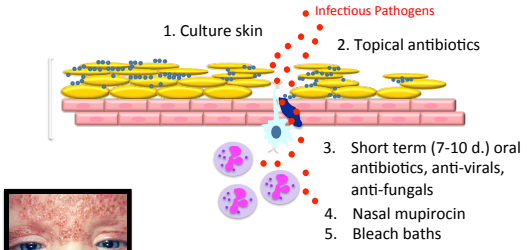
Zinc Oxide Wraps

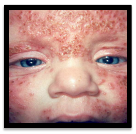
- Recovery of epidermal barrier function
- Antimicrobial
- Provides protective barrier – leave on overnight
- Cover areas with co-flex, mitts, socks, tights, non-latex ace bandage, tubifast

Zinc Oxide Wraps DISADVANTAGES

- Time consuming
- Requires patience and supervision
- Moderate to high expenses for supplies
- Complaints of feeling "Gooey!"

Infections and AD





1. Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/AAAAI/PRACTALL Consensus Report. Adkis CA, et al J Allergy Clin Immunol 2006:118:152-9

Systemic antibiotic choices

<u>Favorites</u>

- Cephalexin (effective, tastes good)
- Dicloxacillin if tablets ok
- Clindamycin or Bactrim for resistant bacteria

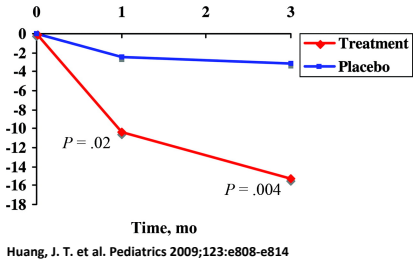
- 7-10 days of antibiotics often sufficient
- Avoid indiscriminate or prolonged use of antibiotics

Dilute Bleach Baths

- Decreases clinical severity of secondary infections and disease severity
- Add 1/4 to 1/2 cup of household bleach to a bath tub full of water three times per week
- Intranasal mupirocin ointment for 5 days
- Burning can occur with open skin
- Use white towels

Huang, JT et al.: Treatment of staphylococcus aureus colonization in atopic dermatitis decreases disease severity. Pediatrics, 2009, 123, e808-e814.

Changes in mean EASI scores over time



Huang, J. T. et al. Pediatrics 2009;123:e808-e814

PEDIATRICS

The Impact of Itch

- Most common problem reported by parents in a chart review study of patients in the AD Center at CHB (LeBovidge et al., 2007)
- Sleep disturbance reported in over 60% of children with AD and their parents and siblings (Chamlin et al., 2005)

Parent Conflict: The Itch-Scratch Cycle

- Parents feel: frustrated, helpless, angry
  - ➔STOP SCRATCHING!!!
  - ➔Giving in"/avoidance of limit setting because the child might scratch
- Children feel: annoyed, ashamed, guilty, angry, frustrated, alone
  - ➔ Increased stress (leads to increased scratching)
  - ➔Scratching in secret

Controlling the Itch

- Cool cloths/ice packs for targeted areas
- Antihistamines:
  - Adequate doses with long half life
  - Sedative effects for evenings
- Common combination:
  - Cetirizine or loratidine during day
  - Hydroxyzine 1mg/kg or diphenhydramine 1mg/kg evening

Team Approach

Externalize the problem

Work as a team against a common problem (i.e., "the itchies")

Methods to Stop Scratching

- Long-sleeved clothing/tights
- Cotton wristbands
- Hands On Activities:
  - Video games (hand-held for car)
  - Novel/special toys used only for diaper changes/ baths/car rides etc

Sleep Disorders in Atopic Dermatitis

- 60-80% incidence in children with AD
- Sequelae: discipline problems, trouble staying awake in afternoon, impaired daytime alertness, parental sleep loss 2.6 hours
- Sleep interventions:
  - Relaxing, **consistent** bedtime routine
  - Wraps
  - Sleep-suits/modified PJ's

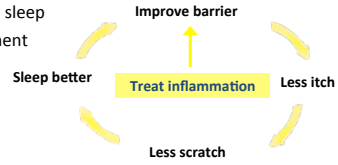
Children's Hospital Boston Atopic Dermatitis Center

- Multidisciplinary outpatient program for children with refractory AD
- Half day session per week
- Treatment team:
  - Nurse Practitioner
  - Psychologist
  - Psychology Intern
  - Nutritionist

www.childrenshospital.org/atopic

Review of AD Center

- 80% of patients had improvement in EASI score
- EASI score improvement correlated with:
  - Improved parental compliance with treatment
  - Decreased parental concern with treatment side effects
  - Decreased itching
  - Better patient sleep
- Cycle of improvement



Ref. Chou J et al. AAAAI 2008 J Allergy Clin Immunol Vol 121;S36

Improve Adherence

- Assess understanding of skincare plan
- Assess concerns about medications
- Assess barriers
  - What are the hardest parts for you/your child to follow?
  - What parts do you skip/miss the most?

Moisturizers

<u>Challenges:</u> He hates the goopy feel! She won't let me put it on! She hates how greasy it is on her face!

- Involve children in the process and make it fun!
  - Apply to mom/dad first
  - Apply to easy to reach areas themselves
  - Draw pictures/letters and rub them in
  - "Frost the cupcake"
  - Set a timer/try to "beat your best time"

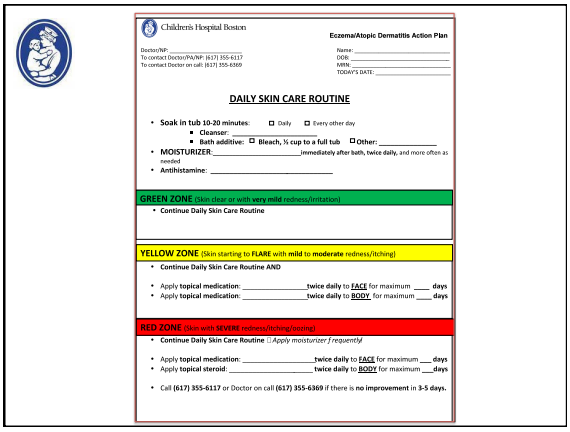
Skin Care Plan

- Patient family education is very important
- Care plan should include:
  - ➢Skin cleansing
  - ➢Skin barrier
  - ➢Control of itching and infection
  - ➢Appropriate use of topical anti-inflammatory agents
  - ➢Elimination of sleep disruption

Evaluation of Eczema Action Plans

- Parents of children with AD given an individualized EAP
- Survey at baseline and follow up done 3 to 12 months after EAP
- 35 children enrolled
- Parental rating of eczema as "severe" decreased from 51% to 3% (p<0.001)

Rork J et al. Eczema Action Plans: a helpful tool in the treatment of pediatric eczema. 2011; submitted.


Children's Hospital Boston

Eczema/Atopic Dermatitis Action Plan

Doctor/NP: _____
To contact Doctor/PA/NP: (617) 355-6117
To contact Doctor on call: (617) 355-6369

Name: _____
DOB: _____
MRN: _____
TODAY'S DATE: _____

DAILY SKIN CARE ROUTINE

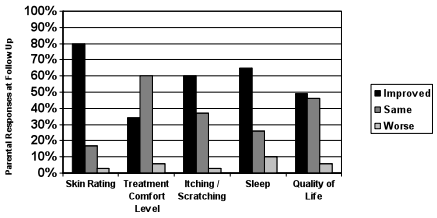
- Soak in tub 10-20 minutes: ☐ Daily ☐ Every other day
  - Cleanser: _____
  - Bath additive: ☐ Bleach, ½ cup to a full tub ☐ Other: _____
- MOISTURIZER: _____ immediately after bath, twice daily, and more often as needed
- Antihistamine: _____

GREEN ZONE (Skin clear or with very mild redness/irritation)
- Continue Daily Skin Care Routine

YELLOW ZONE (Skin starting to FLARE with mild to moderate redness/itching)
- Continue Daily Skin Care Routine AND
- Apply topical medication: _____ twice daily to FACE for maximum ____ days
- Apply topical medication: _____ twice daily to BODY for maximum ____ days

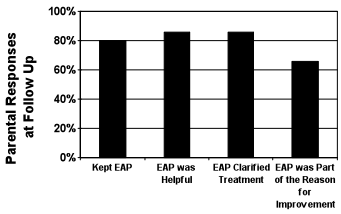
RED ZONE (Skin with SEVERE redness/itching/oozing)
- Continue Daily Skin Care Routine ☐ *Apply moisturizer frequently*
- Apply topical medication: _____ twice daily to FACE for maximum ___ days
- Apply topical steroid: _____ twice daily to BODY for maximum ___ days
- Call (617) 355-6117 or Doctor on call (617) 355-6369 if there is no improvement in 3-5 days.

Comparison of baseline and follow up survey results for AD Action Plan



Rork J et al. Eczema Action Plans: a helpful tool in the treatment of pediatric eczema. 2011; Archives of Dermatology; in press

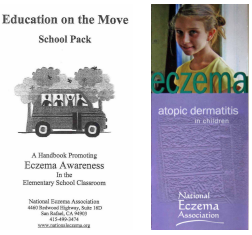
Follow up survey on EAP Effectiveness



Rork J et al. Eczema Action Plans: a helpful tool in the treatment of pediatric eczema. 2011; Archives of Dermatology; in press

Education

- Wet wraps, bleach baths, unna boot instructions can be found on www.eczemacarecenter.com
- Resources
  - National Eczema Assoc Boston support group www.nationaleczema.org
  - ISID www.isidonline.org
  - www.undermyskin.com
  - AAFA
  - FAAN



Treatment & Education Pearls

THERE IS NO EASY ANSWER

We can treat and alleviate, but **we can't cure**.

If something hasn't worked in the past, don't assume it won't work in the future.

Treatment is like juggling. All aspects of disease must be addressed…itch, inflammation, infection and dry skin.

Remind parents! Despite proper skin care and trigger avoidance, **AD may still flare**

Improve barrier:
- Soak and seal
- Barrier creams
- Wet wraps

Avoid Triggers:
- Allergens
-Treat infections
-Keep cool

Control AD
Reduce number and duration of flares

Treat Inflammation:
TCS
- TCI
- Intervene early
- Proactive

Educate Patients:
- Written Plan
- Group programs
- AD education
- Behavior modification

Overview

- Definition
- Treatment
  - Skin care – Soak and seal
  - Anti-inflammatory agents
  - Antibiotics
  - Antipruritics
  - Education
- Triggers: **Role of allergens**

AD Triggers

Infections
URI/OM
Bacterial, fungal, viral skin infections

Allergens
Foods (egg)
Environmental (mites)
Contact (nickel)

Other
Heat, dryness
Anxiety
Vaccinations

Itch-Scratch Cycle & AD Flare

Food Allergy and AD

- FA and AD are highly associated.
  - Up to 37% of children <5 years with moderate to severe AD will have IgE-mediated FA
- Can FA exacerbate AD? *Controversial*
  - Several studies found improvement in pruritus when patients with **egg** allergy and AD were placed on egg-free diet

Lever R et al, Pediatr Allergy Immunol 1998

FA and AD misconceptions

- Eczematous flares can be erroneously attributed to foods by patient/parent
  - May be precipitated by irritants, humidity, change in temperature, infections, etc.

"I want to know what is causing his eczema!"

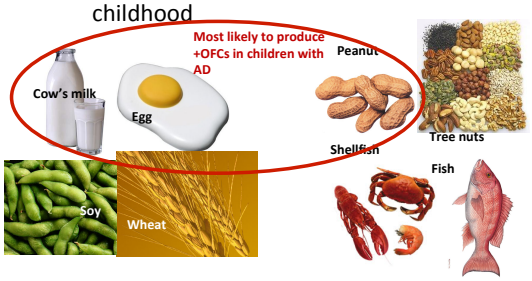
Remind parents! Despite proper skin care and trigger (including food) avoidance,

AD may still flare

Common Food Allergens

Often resolve in childhood

More likely to persist



Uncommon Allergens


Chocolate


Citrus


Berries


Tomato


Corn


Coloring & additives

Testing in children with persistent AD

2010 Food Allergy Guideline 35

- The EP suggests that children less than 5 yrs old with **moderate to severe AD** be considered for FA evaluation for **milk, egg, peanut, wheat, and soy**, if at least 1 of the following conditions are met…

When to consider testing to foods

1. The child has persistent AD **in spite of optimized management and topical therapy**
2. The child has a reliable history of an immediate reaction after ingestion of a specific food

The younger the child and the more severe the AD, the greater likelihood that child has FA

Guillet G & MH, Arch Dermatol 1992

Factors to consider before **reintroducing** foods

- Has food elimination helped AD?
- How long has food been eliminated?
- How long/frequently was food in diet prior to elimination? (Infant or teenager?)
- What testing has been performed?
  - Persons with AD may test positive to many food allergens, but many foods are tolerated (based on oral challenges)

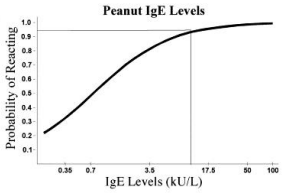
Predictive value of food allergen-specific IgE levels

95% Predictive Level

Allergen	[kU$_A$/L]	PPV
Egg	7	98
- Infants ≤ 2 yrs[+]	2	95
Milk	15	95
- Infants ≤ 2 yrs[++]	5	95
Peanut	14	100
Fish	20	100
Tree nuts[+++]	~15	~95
Soybean	30	73
Wheat	26	74

\+ Boyano MT, et al. Clin Exp Allergy 2001; 31(9):1464-9.
++ Garcia-Ara C, et al. J Allergy Clin Immunol 2001; 107(1):185-90.
+++ Clark AT, Ewan P. Clin Exp Allergy. 2003; 33(8):1041-5

PPV = Positive predictive value



Increasing probability of clinical reactivity with increasing level of food-antigen specific IgE value; note: values <0.35 do not exclude allergic reactivity

Journal of Allergy and Clinical Immunology 2004; 113:805-819

Fleischer et al, J Pediatr 2011

Oral Food Challenges in Children with a Diagnosis of Food Allergy

- Using serum food-specific IgE testing **alone** to diagnose food allergy, especially in children with AD, can result in overly restrictive diet.
- Oral food challenges remain most reliable test for food allergy diagnosis.

Oral Food Challenges (OFCs)

- Retrospective chart review of 125 children with **active atopic dermatitis** and food avoidance evaluated in Denver (National Jewish)

	Total #	% negative OFCs
OFCs	364	89
Foods avoided due to reactions	122	84
Foods avoided due to testing	111	93
Foods avoided for other reasons	131	92

median age 4 years

Atopy Patch Test (APT)

2010 Food Allergy Guideline 8

- NIAID-sponsored EP suggests that APT should **not** be used in routine evaluation of FA
  - No standard reagents available
  - No studies that specifically address APT methodology met inclusion criteria for report
  - Two large studies conclude there is no significant clinical value in using APTs for FA diagnosis

Mehl et al, JACI 2006 & Keskin et al, Ann Allergy Asthma Immunol 2005

"Super high" IgE levels

- Elevated total IgE levels often found in AD
- No studies to date provide support of use of total IgE in interpreting *specific* IgE levels
- Predictive value of ratio of sIgE to total IgE vs. DBPCFC for diagnosis of FA: Ratio offers **no** advantage over sIgE alone. Mehl A et al, Allergy 2005

Allergen Immunotherapy: 3rd update of practice parameter

2011 Summary Statement 8

- There are some data indicating that **immunotherapy can be effective for AD** when associated with aeroallergen sensitivity
- In review of 4 placebo-controlled studies, significant improvement in AD symptoms for patients who received SCIT.

Bussman et al, JACI 2007

House Dust Mite (HDM) Subcutaneous immunotherapy (SCIT)

- Multi-center, randomized, double-blind study of 51 adults with AD
- Maintenance doses of 20, 2000, and 20,000 SQ-U weekly for 1 year
- HDM SCIT effectively **reduced AD** in dose-dependent manner, as measured by SCORAD and topical corticosteroid use

Werfel T et al, Allergy 2006

HDM SCIT – another study

- Open pilot study
- HDM SCIT x 6mos in 25 AD patients +HDMsIgE
- Subjective and objective SCORAD improved significantly within 4 weeks of treatment
- IL-10 levels increased
- CCL17 and IL-16 decreased
- HDM sIgE decreased while sIgG4 increased

Bussman et al, Clin Exp Allergy 2007

HDM Sublingual Immunotherapy (SLIT) for Children with AD/+HDM

- Randomized, double-blind, placebo-controlled
- 48 children (5-16 yrs) with AD (SCORAD >7), stratified by disease severity
- SLIT or placebo for 18 months + standard therapy
- Significant ↓SCORAD and rescue med use found ***only in patients with mild-moderate AD***
- Severe patients had only <u>marginal</u> benefit
- SLIT discontinued in 2 patients because of exacerbation of dermatitis

Pajno et al, JACI 2007 (Italy)

How to treat atopic dermatitis